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EXAMINER
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BERRIOS, JENNIFER A

ART UNIT	PAPER NUMBER
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1619

NOTIFICATION DATE	DELIVERY MODE
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07/15/2009

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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<b>Office Action Summary</b>	<b>Application No.</b> 10/552,030	<b>Applicant(s)</b> GAZZA, GIANLUCA	
	<b>Examiner</b> Jennifer A. Berrios	<b>Art Unit</b> 1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 04 June 2009.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-42 is/are pending in the application.
- 4a) Of the above claim(s) 33-42 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-32 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

This Office Action is in response to Applicant's amendment/remarks/response filed 6/4/2009 wherein claim 1 has been amended.

#### **Response to Arguments**

1. Applicants' arguments, filed 6/4/2009, have been fully considered and are persuasive.
2. The following rejections from the Office action mailed 3/4/2009 are hereby withdrawn as the combination of references fail to teach the ester derivative of hyaluronic acid to not be sulfated, as recited by the newly amended claims:

Claims 1-9, and 16-20 rejected under 35 U.S.C. 103(a) as being unpatentable over US patent 6,027,741 (issued 2/22/2000), cited in IDS on 10/3/2005, in view of US patent 6,579,978 (filed: 4/3/1998).

Claims 11-14 and 17-19 are rejected under 35 USC 103(a) as being unpatentable over US patent 6,027,741 (issued 2/22/2000), cited in IDS on 10/3/2005, in view of US patent 6,579,978 (filed: 4/3/1998), as applied to claims 1-9 and 16-20 above, further in view of US 2002/0082679 (filing date: 11/1/2001)

Claim 24 is rejected under 35 USC 130(a) as being unpatentable over US patent 6,027,741 (issued 2/22/2000), cited in IDS on 10/3/2005, in view of US patent 6,579,978 (filed: 4/3/1998) and US 2002/0082679 (filing date: 11/1/2001) and US patent 6129956 (issued: 10/10/2000), cited in IDS on 10/3/2005, as applied to claims 1-9, 11-14, 16-23, 25-26 and 28-32 above, and further in view of Vercruysse (Critical Reviews in Therapeutic Drug Carrier Systems, 1998).

Claims 10 and 15 are rejected under 35 USC 130(a) as being unpatentable over US patent 6,027,741 (issued 2/22/2000), cited in IDS on 10/3/2005, in view of US patent 6,579,978 (filed: 4/3/1998) and US 2002/0082679, as applied to claims 1-9, 11-14 and 16-20 above, (filing date: 11/1/2001) and further in view of WO 99/03854 (pub date: 1/28/1999, cited on the 10/3/2005 IDS).

Claim 27 is rejected under 35 USC 130(a) as being unpatentable over US patent 6,027,741 (issued 2/22/2000), cited in IDS on 10/3/2005, in view of US patent 6,579,978 (filed: 4/3/1998) and US 2002/0082679 (filing date: 11/1/2001) and US patent 6129956 (issued: 10/10/2000), cited in IDS on 10/3/2005, as applied to claims 1, 6-9, 11-14, 16-23, 25-26 and 28-32 above, and further in view of WO 99/03854 (pub date: 1/28/1999).

3. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application. The limitations of the newly added claims are different in breadth and scope, and therefore the rejections from the previous Office Action, mailed 3/4/2009, have been withdrawn.

With regard to Applicant's remarks regarding the why the Examiner felt that "applicant did not specifically point out the supposed errors in the restriction requirement." Examiner would like to point out that indicating a typographical error in the restriction requirement does not constitute an appropriate traversal, as per the MPEP "the applicant is required to specifically point out the reasons on which **he or she bases his or her conclusions that a requirement to restrict is in error**. A mere

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broad allegation that the requirement is in error does not comply with the requirement of 37 CFR § 1.111 – MPRP 818.03(a)”.

Secondly in the response filed 1/16/2009 applicant states:

Second, the Examiner has argued that Claim 1 lacks a special technical feature and therefore Claim 2-3 and 6-7 lack unity of invention. Applicant has not reviewed the substance of the Examiner's assertion that 6,027,741 in view of the “Biomedical Implants and Devices” article by Shellock renders obvious Claim 1. Should the Examiner reject Claim 1 in view of these two references, Applicant will analyze and respond to the Examiner's rejection. In addition, in the event the Examiner is persuaded that Claim 1 as originally filed or amended is allowable over the prior art, Applicant shall request the Examiner to rejoin Claims 2-3 for examination on the merits.

As such it is clear that the applicant has not responded to the Examiner's rejection and furthermore when arguing that Claim 1 lacks a special technical feature in view of the prior art cited above, Examiner is arguing that Group I and Groups II-III lack a special technical feature and as such a restriction requirement is appropriate.

Regarding the election of species, Examiner is not arguing that claims 3-4 and 6-7 lack unity of invention, however the Markush group of alcohols listed do lack a special technical feature amongst them, as such a requirement to elect a specific species is proper, as per MPEP 1850. Examiner would like to also point out that Claims 2 and 3 were never withdrawn from consideration and were considered and examined in the office action mailed 3/4/2009.

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***Claim Rejections - 35 USC § 103***

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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5. Claims 1-9, and 16-20 rejected under 35 U.S.C. 103(a) as being unpatentable over US patent 6,027,741 (issued 2/22/2000), cited in IDS on 10/3/2005, US patent 6,579,978 (filed: 4/3/1998) and US Patent 4,851,521 (issued: 7/25/1989).

Claims 1-3 teach a stent comprising a coating of a ester derivative of hyaluronic acid (HA) polymer, in which the ester derivative has all or some carboxyl groups selected from the aliphatic, arylaliphatic, and other; more specifically from the benzyl alcohol series. Claims 4-7 further limit claim 1 by defining the degree of esterification of the hyaluronic acid ester derivative which varies from 50-100%, 70-100%, 100% and 75% of the carboxyl groups of the HA. Claims 8-9 further limit claim 1 by teaching that the stent has a pharmacologically active ingredient associated with the HA polymer coating, the active ingredient selected from an anti-inflammatory, anti-proliferative, anti-migratory and an immunosuppressant. Claims 16-19 teach that the stent comprising an active ingredient and HA are released from the HA polymer coating, with the coating have a thickness of .5-40 microns, preferably of 5-10 microns, over a prolonged period of time, or after one month and within 2 weeks. Claim 20 teaches the stent of claim 1 comprising a layer of HA bound to the stent and a coating of HA polymer.

The '741 patent teaches a coated biomedical object or device having a coating of sulfated polysaccharide, wherein the polysaccharide is a hyaluronic acid, hyaluronate ester or a salt thereof, Specifically a sulfated hyaluronate ester (column 16, claims 1 and 4). The '741 patent further teaches that important derivatives of hyaluronic acid are esters thereof with alcohol of the aliphatic, arylaliphatic, heterocyclic and cycloaliphatic series (Column 2, Lines 35-45). US '741 further explain examples of sulfated hyaluronic

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acid ester that can be used in the present invention. Examples of such include HYAFF 11 (meaning 100% of the carboxyl groups are in the form of benzyl esters) (Column 4, lines 38-43); HYAFF 11p75 (75% benzyl ester of HA) (Column 7, lines 55-58).

US '741 also teaches that pharmaceutical preparations and biomaterials comprising sulfated derivatives of HA can be administered alone or in association with other chemical polymers and/or pharmacologically acceptable drugs (column 14, example 16). Examples include the association of a sulfated HA and a HA ester (non-sulfated) with an antibiotic, anti-inflammatory, antimicrobial, antibacterial and more (Column 15, lines 15-20).

The '741 patent fails to teach what constitutes a biomedical object or device and also fails to teach the ester derivative of the hyaluronic acid to not be sulfated

. The '978 patent teaches biomaterials comprising sulphated hyaluronic acid compounds and derivatives thereof (Claim 1 and 13), wherein the derivative is selected from the group consisting of a partial or total ester (claim 14). The biomaterials can be used to advantage in various fields of surgery, such as in the preparation of cardiac valves and vascular stents (column 5, lines 66-67-column 6, lines 4-5).

The '521 patent teaches non-sulphated esters of hyaluronic acid in which all or only a portion of the carboxylic groups of the acid are esterified and the salts of the partial esters with pharmacologically acceptable organic bases. Pharmaceutical preparation contain a active ingredient, one or more hyaluronic acid esters or a salt there of and a pharmacologically active substance. These can be used in medicine, surgery or cosmetics (Abstract). Alcohols of the aliphathic, araliphatic series can be



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used as esterifying components of the carboxylic groups of hyaluronic acid. Special attention should be give to benzyl alcohol and phenetyl alcohol (Column 9 lines 25-30 - Column 10 lines 25-37). Of particular interest is those partial esters in which at least 5% and at most 90% of all the carboxylic groups of HY are esterified (Column 9, 39-43).

A vast selection of chemotherapeutic agents can be used for treatment and administered orally or systematically, often in association with steroidal anti-inflammatory agents (Column 12, lines 10-15).

HA may be used as an additive for a wide variety of polymeric materials for use in medical and surgical articles. The addition of HA or one of it's salts is effected by covering the surface of such materials, these material can be used for the manufacture of cardiac valves, vascular clips, pacemakers, etc (Column 2, lines 10-20).

Table 1 of the '521 patent describes 9 HA carboxyl's esterified with corticosteroid. Of these nine, 3 were dissolved in DMSO and the remaining 6 were dissolved in saline. These preparations were administered by instillation in the right eye of rabbits. Results showed that all preparations were effective at reducing inflammation.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to combine the teaching of the '741, '521 patent and the '978 patent. One of ordinary skill in art would have been motivated to substitute a stent for a biomedical object, because it was well known at the time of the invention that stents comprising sulphonated hyaluronic acid compounds and derivatives thereof, are advantages in various fields of surgery, as these compounds have anticoagulant and antithrombotic activities (see Abs. of Patent '978). Furthermore, one of ordinary skill in the art would

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have been motivated to create medical devices comprising non-sulfated HA ester derivatives as it was well known in the art at the time the invention was made that these could be used in conjunction with polymeric materials and therapeutic agents for the preparation of medical and surgical articles, as demonstrated by patents '741 and '521. One of ordinary skill in the art would have been motivated to substitute two equivalents, in this case HA ester derivatives, whether sulfated or non-sulfated, which are taught by the prior art to be useful for the same purpose. Finally one of skill in the art would expect to be reasonable successful because both patents ;741 and '521 teach HA ester or salts there of, whose carboxylic groups are esterified with alcohols selected from aliphatic, arylaliphathic, cycloalipathic and heterocyclic series.

The '741 patent also fails to teach the time period for the release of the HA and the active ingredient from the HA polymer coating. As the stent described in the instant claim 1 comprises the same coating and HA as the biomedical device of the '741 patent it is expected that the properties of the devices be the same. Therefore the device of the '741 patent would have the same expectancy of release as the stent of instant claim 1.

The above mentioned prior art also fails to teach the thickness of the polymer coating. Since the above art teaches the stent of instant claim 1, it would be obvious to one of ordinary skill to determine the optimum thickness of the HA polymer coating, that would be the most effective.

Therefore Claims 1-9 and 16-20 are rejected under 35 USC 103(a) as being unpatentable over the prior art.

6. Claims 11-14 and 17-19 are rejected under 35 USC 103(a) as being unpatentable over US patent 6,027,741 (issued 2/22/2000), cited in IDS on 10/3/2005, US patent 6,579,978 (filed: 4/3/1998) and US Patent 4,851,521 (issued: 7/25/1989), as applied to claims 1-9 and 16-20 above, further in view of US 2002/0082679 (filing date: 11/1/2001)

US patents '741, '521 and '978 teach the limitation of instant claims 11-14 and 17-19, however they fail to teach the further limitations of each set of claims. Instant claims 11-14 further limit the teachings of the stent of instant claim 1 comprising an active ingredient associated with the HA polymer coating in the quantity between .001mg and 10mg for the following actions: anti-inflammatory, anti-migratory, anti-proliferative and immunosuppressant. While, Claims 17-19 further teach that the stent comprising an active ingredient and HA are released from the HA polymer coating, over a prolonged period of time, or after one month and within 2 weeks. US 2002/0082679 provide a luminal prosthesis, such as vascular stents and grafts for reducing or inhibiting restenosis (Paragraph 0003). The luminal prosthesis allows for the programmed and controlled substance delivery of therapeutic agents (Paragraph 0028). Therapeutic agents may be selected from a group consisting of immunosuppressants, anti-inflammatory, anti-proliferatives, and anti-migratory agents, among others (Paragraph 0029). It also teaches that the source of the therapeutic agent is a polymeric material including therapeutic capable moieties as a structural subunit of the

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polymer (Paragraph 0031). The prosthesis incorporates the substance by coating the substance on the prosthesis (Pg 21, claim 15). The total amount of the therapeutic agent is generally from .1 micrograms to 10g, but is preferably .1 micrograms to 10mg. This therapeutic agent may be released in a time period, as measured from the time of implanting the device, ranging from 1-200 days, 1-45 days and 7-21 days.

US 2002/0082679 fails to teach the properties of luminal prosthesis to be those of the stent of the instant claims. However, the '741 patent, as applied to claims 1-9 and 16-20 above does teach the properties of the medical device.

It would be *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute the polymer and therapeutic coating as taught in US 2002/0082679 for the HA polymer coating and active agent taught in the '741 patent. One of ordinary skill in the art would be motivated to substitute two equivalents, in this case polymers, which are taught by the prior art to be useful for the same purpose. Finally, a person of skill in the art would reasonably have expected to be successful because both references disclose biomedical objects comprising a polymer coating that contain an active therapeutic agent.

7. Claims 20-23, 25-26 and 28-32 are rejected under 35 USC 130(a) as being unpatentable over US patent 6,027,741 (issued 2/22/2000), cited in IDS on 10/3/2005, US patent 6,579,978 (filed: 4/3/1998), US Patent 4,851,521 (issued: 7/25/1989), and US 2002/0082679, as applied to claims 1-9, 11-14 and 16-20 above, (filing date:

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11/1/2001) and further in view of US patent 6129956 (issued: 10/10/2000), cited in IDS on 10/3/2005.

The US patents '741, '521 and '978 teach the limitations of claims 20-23, 25-26 and 28-32, however fail to teach further limitations set forth by each set of claims. Claims 21-23 and 32 teach the stent of instant claim 1, further comprising a second coating of a polymer of hydrophobic nature, having a contact angle with water greater than 60°, applied directly to the surface of the stent. Claim 25 further specifies that the polymer of hydrophobic nature is polystyrene. Claims 26, 28 - 30 explain that the hydrophobic polymer, with a thickness of .5-40 micron, preferably 5-10 microns, is associated with an active ingredient (anti-inflammatory, anti-proliferative, anti-migratory and/or immunosuppressant). Said active ingredient is available in quantities between .0001mg and 10mg, and is released over a period of one month. Claim 31 teaches that the active coating of the two polymer coatings can be the same or different.

The '741 and the '521 patent fail to teach whether the coated vascular stents contain one or more coating and the degree of contact with water for the hydrophobic polymer.

The '956 patent teaches a process for coating objects, for surgical, diagnostic and healthcare fields, with HA and derivatives thereof (see abstract). The '959 patent (column 14, example 11) takes a sample of polystyrene (hydrophobic polymer) from a bacteriological grade Petri dish and treats it with plasma. This treated sample is then dipped and extracted from the following solutions: 1% HA acid; 1%HA and 1% 3-aminopropyltrimethoxy silane plus others; 1% HA 50% esterified with benzyl alcohol

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and 3-aminopropyltrimethoxy silane plus others. The contact degree with water of polystyrene although not specifically stated can be expected to have the same properties as disclosed by the applicant since the polymers are equivalents to one another.

The above mentioned prior art also fails to teach the thickness of the polymer coating. Since the above art teaches the stent of instant claim 1 with the limitations of claim 21, it would've been *prima facie* obvious to one of ordinary skill at the time the invention was made to determine the optimum thickness of the HA polymer coating, that would be the most effective.

US 2002/0082679 teaches polymeric material on a stent containing therapeutic agents. US '741 teaches a stent with HA polymer coating which can additionally contain active agents and the '956 patent teaches an object coated with polymeric material (polystyrene) and HA polymer coating, although no mention of therapeutic agents are made. However as taught above in US 2002/0082679 the source of the therapeutic agents associated with vascular stent coatings are polymers.

One of ordinary skill in the art at the time the invention was made would have been motivated to combine the teaching of US 2002/0082679, the '741 and '521 patent and the '956 patent since both the '741 patent and the '956 patent teaches stents coated with polymers and the '741 patent teaches that these polymers could contain therapeutic agents. It would be obvious to one of ordinary skill, as these two compositions are taught by the prior art to be useful for the same purpose and therefore

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it would be obvious to combine the two to form a third composition for the same purpose.

8. Claim 24 is rejected under 35 USC 130(a) as being unpatentable over US patent 6,027,741 (issued 2/22/2000), cited in IDS on 10/3/2005, US patent 6,579,978 (filed: 4/3/1998), US Patent 4,851,521 (issued: 7/25/1989), US 2002/0082679 (filing date: 11/1/2001) and US patent 6,129,956 (issued: 10/10/2000), cited in IDS on 10/3/2005, as applied to claims 1-9, 11-14, 16-23, 25-26 and 28-32 above, and further in view of Vercruysse (Critical Reviews in Therapeutic Drug Carrier Systems, 1998).

The US patents '741, '521, '978 and '959 teach the limitations of claim 24, however they fail to teach the further limitation set forth by the claim. Claim 24 further teaches the second coating of the stent of instant claim 21 to be polymethyl methacrylate among others, with a contact degree angle with water of 60°. The above teachings fail to specify one of the exact polymers given in claim 24. The above art teaches a polystyrene coated with HA and derivatives thereof, while Vercruysse specifically teaches polymethyl methacrylate coated with HA (pg 528, lines 5-9).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute polystyrene for polymethyl methacrylate since the prior art teaches these to be equivalents, both hydrophobic and both are coated with HA. The contact degree with water of polystyrene although not specifically stated can

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be expected to have the same properties as disclosed by the applicant since the polymers can be considered equivalents to one another.

9. Claims 10 and 15 are rejected under 35 USC 130(a) as being unpatentable over US patent 6,027,741 (issued 2/22/2000), cited in IDS on 10/3/2005, US patent 6,579,978 (filed: 4/3/1998), US Patent 4,851,521 (issued: 7/25/1989), and US 2002/0082679, as applied to claims 1-9, 11-14 and 16-20 above, (filing date: 11/1/2001) and further in view of WO 99/03854 (pub date: 1/28/1999, cited on the 10/3/2005 IDS).

The US patents '741, '521 and '978 and the '679 publication teach the limitations of claims 10 and 15, however fail to teach further limitations set forth by each claim. Claims 10 and 15 further teach that the active agent associated with the stent of instant claim one is specifically 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate.

US 2002/0082679 and the '741 and '521 patent teach the stent of instant claim 1 with an active agent, with quantities preferably of .1 micrograms to 10mg. What they fail to teach is the active ingredient being 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate.

WO 99/03854 teaches that 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate is effective in diseases associated with vascular smooth-muscle migration and proliferation, such as restenosis and atherosclerosis (pg 12, lines 25-27). As such 4-[(4-methyl-1-



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piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate can thus inhibit proliferation and especially the migration of vascular smooth-muscle cells (pg 16, lines 1-3).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of WO 99/03854 with US 2002/0082679, the '741, '521 and the '978 patents as it was well known at the time of the invention the properties of 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate and it would be obvious to use this compound as an active agent in a medical stent to treat restenosis.

10. Claim 27 is rejected under 35 USC 130(a) as being unpatentable over US patent 6,027,741 (issued 2/22/2000), cited in IDS on 10/3/2005, US patent 6, 579,978 (filed: 4/3/1998), US Patent 4,851,521 (issued: 7/25/1989), and US 2002/0082679 (filing date: 11/1/2001) and US patent 6129956 (issued: 10/10/2000), cited in IDS on 10/3/2005, as applied to claims 1, 6-9, 11-14, 16-23, 25-26 and 28-32 above, and further in view of WO 99/03854 (pub date: 1/28/1999).

The US patents '741, '521 and '978 and '956 and the '679 publication teach the limitations of claim 27, however fail to teach the further limitations set forth the claim. Claim 27 further teaches that the active agent associated with the stent of instant claim 21 is specifically 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate.

The above teaching fails to teach this exact active ingredient as the therapeutic agent. WO 99/03854 teaches that 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate is effective in diseases associated with vascular smooth-muscle migration and proliferation, such as restenosis and atherosclerosis (pg 12, lines 25-27). As such 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate can thus inhibit proliferation and especially the migration of vascular smooth-muscle cells (pg 16, lines 1-3).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of US patents '741, '521 and '978 and '956 and the '679 publication with WO 99/03854 as it was well known at the time of the invention the properties of 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate and it would be obvious to use this compound as an active agent in a medical stent to treat restenosis.

### ***Conclusion***

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

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§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer A. Berríos whose telephone number is (571)270-7679. The examiner can normally be reached on Monday-Thursday: 7:00am-4:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JB

/MP WOODWARD/  
Supervisory Patent Examiner, Art Unit 1615